Claims:

1. A method of identifying a gene associated with a desired behavior in a mammal, comprising the steps of:

(a) Providing a test population of mammals having the desired behavior;

(b) Providing a control population of mammals lacking the desired behavior;

(c) Isolating and pooling expressed RNA from neural tissue of the test population;

(d) Isolating and pooling expressed RNA from neural tissue of the control population;

(e) Determining the level of expression of a plurality of genes in each of the RNA pools created in steps (c) and (d); and,

(f) Selecting a gene from the plurality of genes, the expression of which differs between the test population and the control population of mammals, wherein the selected gene is a candidate gene associated with said desired behavior.

2. A method of identifying a gene associated with cognitive function in a mammal, comprising the steps of:

(a) Providing a test population of mammals having a desired cognitive function;

(b) Providing a control population of mammals impaired in such cognitive function;

(c) Isolating and pooling expressed RNA from neural tissue of the test population;

(d) Isolating and pooling expressed RNA from neural tissue of the control population;

(e) Determining the level of expression of a plurality of genes in each of the RNA pools created in steps (c) and (d); and,

(f) Selecting a gene from the plurality of genes, the expression of which differs between the test population and the control population of mammals, wherein the selected gene is a candidate gene associated with cognitive function.

3. The method of claim 1 or 2 wherein the level of expression of said plurality of genes is detected by a method selected from the group consisting of: microarray analysis, in situ hybridization histochemistry, quantitative PCR, SAGE analysis, Northern blot analysis, and dot blot analysis.

4. The method of claim 1 or 2 wherein said plurality of genes comprises a gene involved in glutamate transport.

5. The method of claim 4 wherein said gene involved in glutamate transport is selected from the group consisting of: EAAT1, EAAT2, EAAT3, EAAT4, and EAAT5.

6. The method of claim 1 or 2 wherein said plurality of genes comprises a gene other than a glutamate transporter selected from the group consisting of: EAAT1, EAAT2, EAAT3, EAAT4, and EAAT5.

7. A method of screening compounds for utility in promoting cognitive function, comprising the steps of:

(a) Administering a test compound to a mammal;

(b) Determining the level of expression of a gene in neural tissue of said mammal following administration of said test compound;

(c) Comparing said level of expression of said gene to a reference level of expression thereof in neural tissue of a mammal to whom said test compound was not administered; and,

(d) Determining whether the level of expression of said gene differs from the corresponding reference level of expression thereof, wherein said difference indicates that the test compound is a candidate therapeutic agent for promoting cognitive function.

8. The method of claim 7 comprising the further step of comparing said level of expression of said gene to a reference level of expression thereof in neural tissue of a mammal to whom ceftriaxone was administered.

9. The method of claim 7 wherein the level of expression of said gene is detected by a method selected from the group consisting of: microarray analysis, in situ hybridization histochemistry, quantitative PCR, SAGE analysis, Northern blot analysis, and dot blot analysis.

10. The method of claim 7 wherein said gene is a glutamate transporter.

11. The method of claim 10 wherein said gene is selected from the group consisting of: EAAT1, EAAT2, EAAT3, EAAT4, and EAAT5.

12. The method of claim 1, 2 or 7 wherein said neural tissue is hippocampal tissue.

13. A method of screening compounds for utility in promoting cognitive function, comprising the steps of:

(a) Administering a test compound to a mammal;

(b) Determining the level of expression of a glutamate transporter gene in neural tissue of said mammal following administration of said test compound;

(c) Comparing said level of expression of said gene to a reference level of expression thereof in neural tissue of a mammal to whom said test compound was not administered; and,

(d) Determining whether the level of expression of said gene differs from the corresponding reference level of expression thereof, wherein said difference indicates that the test compound is a candidate therapeutic agent for promoting cognitive function.

14. A method of screening compounds for utility in promoting cognitive function in a mammal, comprising the steps of:

(a) Contacting a test compound with a cell expressing a gene listed in Figure 4; and

(b) Determining whether the level of expression of said gene is changed by contact of said cell with said test compound, said change if present being indicative of the ability of said compound to promote cognitive function in a mammal in need thereof.

15. The method of claim 14 wherein said cell is derived from neural tissue.

16. The method of claim 15 wherein said cell is an immortalized cell.

17. The method of claim 16 wherein said cell is a neuronal cell line, a glial cell line, or an astrocyte cell line.

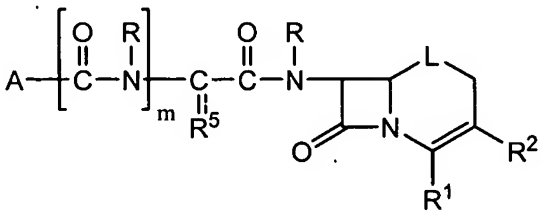
18. The method of claim 14 wherein said gene is a glutamate transporter.

19. The method of claim 1, 2, 7, 13, or 14 wherein the level of expression of said gene is increased.

20. The method of claim 1, 2, 7, 13, or 14 wherein the level of expression of said gene is decreased.

21. The method of claim 7, 13, or 14 wherein said test compound is a small molecule.

22. The method of claim 21 wherein said test compound is:



I

wherein, individually for each occurrence:

L is O or S;

R is H, $C_{1\text{-}10}$ alkyl, $C_{1\text{-}10}$ alkoxy, aryl, aralkyl, $-OCH_2CO_2H$;

R^1 is $-(CH_2)_n-C(O)X$

wherein

X is OH, NR_2, SH, O-alkali metal, or $-OC(CH_3)OC(O)OCH(CH_3)_2$; and

n is an integer from 0 to 6 inclusive;

R^2 is H, C_{1-10} alkyl, C_{2-8} alkenyl, or $-(CH_2)_a-W-R^3$

wherein

R^3 is H, C_{1-10} alkyl, $-C(O)C_{1-10}$ alkyl, $-C(O)NR_2$, aryl, aralkyl, or A;

W is O, S, or NR^4; and

a is an integer from 1 to 6 inclusive;

wherein

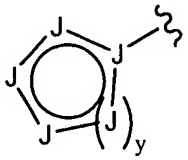
R^4 is H, C_{1-10} alkyl, $-C(O)C_{1-10}$ alkyl, aryl, aralkyl, or R^3 and R^4 taken together may form an unsubstituted or substituted heteroalkyl or heteroaryl ring;

the ---- line indicates either a single or double bond;

R^5 is R^1, H, SO_3H, aryl, C_{1-10} alkyl, aralkyl; or R^5 is selected from the group consisting of $=CHCH_2CO_2H$ and =NR when the ---- line is a double bond;

m is 0 or 1; and

A is aryl or heteroaryl of formula **Ia**:



Ia

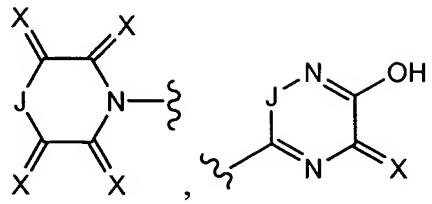
wherein, independently for each occurrence:

J is O, S, NR^6, or CR^6; and

y is 1 or 2;

wherein R^6 is an electron pair, H, C_{1-10} alkyl, C_{1-10} alkoxy, aryl, or $-NR_2$;

or A is heterocycloalkyl of formula **Ib** or **Ic**:



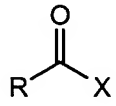
Ib **Ic**

wherein, independently for each occurrence:

J is O, S, or NR; and

X is O or H_2.

23. The method of claim 21 wherein said test compound is:



II

wherein, independently for each occurrence:

X is -OH, C_{1-10} alkoxy, -O-alkali metal, -$N(R^1)_2$, -SH, or -S-C_{1-10} alkyl;

R is a straight chain or branched C_{1-30} alkyl; and

R^1 is H, C_{1-10} alky, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, or aralkyl;

provided that R may be unsubstituted or substituted by one or more -OH, C_{1-10} alkoxy, -$N(R^1)_2$, -SH, -S-C_{1-10} alkyl, or aryl.

24. A library comprising a plurality of cDNA sequences coding for genes that are differentially expressed in neural tissue upon preservation of cognitive function in a mammal.

25. A library comprising a plurality of cDNA sequences coding for genes that are differentially expressed in neural tissue upon treatment of a mammal with ceftriaxone.

26. A library comprising a plurality of cDNA sequences coding for genes that are differentially expressed in neural tissue upon treatment of a mammal with valproic acid.

27. The library of claim 24, 25 or 26 wherein said plurality of cDNA sequences comprises a sequence derived from a glutamate transporter gene.

28. The library of claim 27 wherein said glutamate transporter gene is selected from the group consisting of: EAAT1, EAAT2, EAAT3, EAAT4, and EAAT5.

29. The library of claim 27 wherein said plurality of cDNA sequences comprises at least 20% of all sequences present therein.

30. The library of claim 27 wherein said plurality of cDNA sequences comprises at least 50% of all sequences present therein.

31. The library of claim 27 wherein said plurality of cDNA sequences comprises at least 80% of all sequences present therein.

32. A microarray chip comprising a solid support having attached thereto, at individually addressed locations, cDNA sequences corresponding to members of the library of claims 24, 25 or 26.

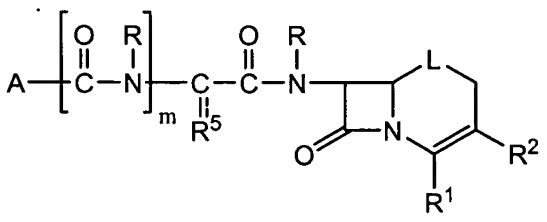
33. A pharmaceutical composition comprising a therapeutically effective amount of a compound that stimulates neural tissue expression of a gene listed in Figure 4.

34. The pharmaceutical composition of claim 33 wherein said gene is a glutamate transporter.

35. The pharmaceutical composition of claim 34 wherein said glutamate transporter is EAAT1, EAAT2, EAAT3, EAAT4, or EAAT5.

36. The pharmaceutical composition of claim 33 wherein said compound is a small molecule.

37. A pharmaceutical composition comprising a therapeutically effective amount of:



I

wherein, individually for each occurrence:

L is O or S;

R is H, C_{1-10} alkyl, C_{1-10} alkoxy, aryl, aralkyl, $-OCH_2CO_2H$;

R^1 is $-(CH_2)_n-C(O)X$

wherein

X is OH, NR_2, SH, O-alkali metal, or $-OC(CH_3)OC(O)OCH(CH_3)_2$; and

n is an integer from 0 to 6 inclusive;

R^2 is H, C_{1-10} alkyl, C_{2-8} alkenyl, or $-(CH_2)_a-W-R^3$

wherein

R^3 is H, C_{1-10} alkyl, $-C(O)C_{1-10}$ alkyl, $-C(O)NR_2$, aryl, aralkyl, or A;

W is O, S, or NR^4; and

a is an integer from 1 to 6 inclusive;

wherein

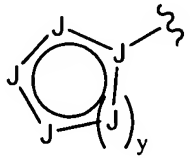
R^4 is H, C_{1-10} alkyl, $-C(O)C_{1-10}$ alkyl, aryl, aralkyl, or R^3 and R^4 taken together may form an unsubstituted or substituted heteroalkyl or heteroaryl ring;

the ---- line indicates either a single or double bond;

R^5 is R^1, H, SO_3H, aryl, C_{1-10} alkyl, aralkyl; or R^5 is selected from the group consisting of $=CHCH_2CO_2H$ and =NR when the ---- line is a double bond;

m is 0 or 1; and

A is aryl or heteroaryl of formula **Ia**:



Ia

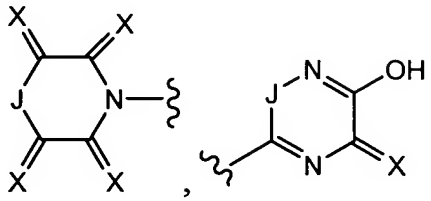
wherein, independently for each occurrence:

J is O, S, NR^6, or CR^6; and

y is 1 or 2;

wherein R^6 is an electron pair, H, C_{1-10} alkyl, C_{1-10} alkoxy, aryl, or $-NR_2$;

or A is heterocycloalkyl of formula **Ib** or **Ic**:



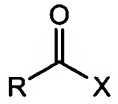
Ib **Ic**

wherein, independently for each occurrence:

J is O, S, or NR; and

X is O or H_2.

38. A pharmaceutical composition comprising a therapeutically effective amount of:



II

wherein, independently for each occurrence:

X is -OH, C_{1-10} alkoxy, -O-alkali metal, $-N(R^1)_2$, -SH, or $-S-C_{1-10}$ alkyl;

R is a straight chain or branched C_{1-30} alkyl; and

R^1 is H, C_{1-10} alky, C_{2-10} alkenyl, C_{2-10} alkynyl, aryl, or aralkyl;

provided that R may be unsubstituted or substituted by one or more -OH, C_{1-10} alkoxy, $-N(R^1)_2$, -SH, $-S-C_{1-10}$ alkyl, or aryl.

39. A pharmaceutical composition comprising a therapeutically effective amount of a therapeutic agent, other than ceftriaxone or valproic acid, identified according to the method of claim 7, 13, or 14.

40. A method of preserving cognitive function in a mammal in need thereof, comprising the step of stimulating, in said mammal, neural tissue expression of a glutamate transporter gene.

41. A method of treating impaired cognitive function in a mammal, comprising the step of stimulating, in said mammal, neural tissue expression of a glutamate transporter gene.

42. A method of preserving cognitive function in a mammal in need thereof, comprising the step of administering a pharmaceutical composition of claim 33 to said mammal.

43. A method of preserving cognitive function in a mammal in need thereof, comprising the step of administering a pharmaceutical composition of claim 37 to said mammal.

44. A method of preserving cognitive function in a mammal in need thereof, comprising the step of administering a pharmaceutical composition of claim 38 to said mammal.

45. A method of preserving cognitive function in a mammal in need thereof, comprising the step of administering a pharmaceutical composition of claim 39 to said mammal.

46. The method of claim 43, wherein said mammal is free of symptoms of an infectious disease for which antibiotic treatment is indicated.

47. A method of promoting cognitive function in a mammal in need thereof, comprising administering to said mammal an amount of a pharmaceutical composition of claim 33 sufficient to promote cognitive function selected from the group consisting of: spatial memory acquisition, long-term spatial memory and spatial memory retrieval.

48. A method of preserving cognitive function in an aged mammal, comprising the step of administering a therapeutically effective amount of ceftriaxone or an analog or derivative thereof to said mammal.

49. A method of treating impaired cognitive function in a mammal, comprising the step of administering a therapeutically effective amount of ceftriaxone or an analog or derivative thereof to said mammal.

50. The method of claim 41 or 49 wherein said impaired cognitive function is a condition selected from the group consisting of: mild cognitive impairment, age related cognitive decline, memory loss, senility, and dementia .

51. The method of claim 41 or 49 wherein said impaired cognitive function is Alzheimer's Disease.

52. The method of claim 41 or 49 wherein said mammal is human.

53. The method of claim 40, 42, 43, 44, 45, 46, 47, or 47 wherein said mammal is human.